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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,925	12/04/2006	Peter J. Wettstein	07039-501US1	1016

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
08/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,925	WETTSTEIN ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7 and 10-1620* is/are pending in the application.

4a) Of the above claim(s) *7-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6, 8, 16, 20, 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and response filed 5/6/10 is acknowledged and has been entered.

The Declaration of Inventor Heather A. Hardin under 37 C.F.R. 1.131 filed 5/6/10 is acknowledged and has been entered.

The Declaration of Inventor Michael A. Strausbauch under 37 C.F.R. 1.131 filed 5/6/10 is acknowledged and has been entered.

The Declaration of Inventor Peter J. Wettstein under 37 C.F.R. 1.131 filed 5/6/10 is acknowledged and has been entered.

The Declaration of Inventor Nancy D. Borson under 37 C.F.R. 1.131 filed 5/6/10 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election without traverse of Group I and the species of CTL-activating amino acid sequence SEQ ID NO: 9, CpG-interacting amino acid sequence SEQ ID NO: 2 and a CpG molecule comprising at least one sulfur atom SEQ ID NO: 8 comprising a phosphorothioate linkage in Applicant's responses filed 6/3/09 and 8/18/09.

Claims 1, 3, 13, 16, 20 and 24 read upon the elected species.

Applicant is reminded that upon consideration of the prior art, examination had been extended to include the species recited in instant claims 2, 6 and 8.

Claims 1-3, 6, 8, 13, 16, 20 and 24 are currently being examined.

3. The above-listed Declarations of each of the Inventors, all filed on 5/6/10 under 37 CFR 1.131 is sufficient to overcome the Schirmbeck *et al* (J. Immunol. 2003, 171: 5198-5207) reference that was cited in the prior rejection of record of claims 1-3, 6, 8, 9, 16, 20 and 24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schirmbeck *et al* (J. Immunol. 2003, 171: 5198-5207, IDS reference) in view of Vives *et al* (J. Biol. Chem. 1997, 272(25): 1610-1617, IDS reference).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 6, 8, 9, 16, 20 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lingnau *et al* (Vaccine 2002, 20: 3498-3508) in view of Liu (PNAS 1997, 94: 10496-10498) , Vives *et al* (J. Biol. Chem. 1997, 272(25): 1610-1617, IDS reference) and Vabulas *et al* (J. Immunol. 2000, 164: 2372-2378).

Lingnau *et al* teach a composition comprising a T cell epitope peptide for class I MHC (*i.e.,* a CTL epitope), a poly-Arg peptide, and CpG-ODN, and that the addition of the cationic peptide and CpG-ODN with the T cell epitope peptide led to enhanced peptide-specific immune responses, as cationic poly-amino acids , including poly-Arg and poly-Lys, enhance the uptake of CTL epitope peptides into antigen presenting cells (APCs) both *in vitro* and *in vivo*. The inclusion of both CpG-ODN, which activates APCs, and poly-Arg induced much more potent immune responses than peptide vaccine containing either one of these immunomodulators alone. Lingnau *et al* teach that the opposite charge of the CpG-ODN and the poly-Arg support their electrostatic interaction, *i.e.,* their association (to a Cp-G-interacting amino acid sequence) (see entire reference, especially abstract, introduction, section 2.4 at lines 4-12 and discussion section).

Lingnau *et al* do not teach wherein the CpG-ODN comprises sulfur, including a phosphorothioate linkage, nor wherein the T cell epitope peptide is fused to the CpG-interacting amino acid sequence, nor wherein the CpG-interacting sequence comprises at least one cysteine residue.

Liu teaches using a fusion polypeptide comprising a CTL epitope and a polypeptide that translocates the peptide into the cytoplasm of a cell as a strategy to deliver CTL epitopes for processing and presentation of the CTL epitope by class I MHC in an APC (entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a fusion polypeptide of the CTL epitope and the poly-Arg translocating peptide taught by Lingnau *et al* in the composition of Lingnau *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to further enhance uptake of the CTL epitope peptide by making the process more efficient by keeping both peptides associated with one another, particularly in light of the teaching of both references that the translocating peptide facilitates translocation of the CTL epitope and the teaching of Liu that such fusion polypeptides may be made for the same purpose.

Vives *et al* teach that the Tat 48-60 peptide (CGRKKRRQRRRPPQC) with both a N- and a –C-terminal cysteine and with or without the three carboxy-terminal amino acid residues (CGRKKRRQRRRC) induced good intracellular translocation of the peptide. Vives *et al* further teach coupling to peptides, proteins, oligonucleotides or peptide-nucleic acids to improve the cellular uptake and induce a biological activity (see entire reference, especially abstract, materials and methods, and discussion section).

Vabulas *et al* teach compositions comprising MHC class I-restricted T cell epitopes and phosphorothioate-stabilized CpG-ODN, and that the T cell epitope peptides are not immunogenic unless aided by an adjuvant such as the CpG-ODN (especially abstract, introduction and first paragraph of materials and methods section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted any cationic translocating peptide such as the Tat peptide taught by Vives *et al* for the poly-Arg peptide taught by Lingnau *et al*, and to have substituted any equivalent or better CpG-ODN such as the phosphorothioate-stabilized CpG-ODN taught by Vabulas *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to enhance the immune response to a CTL epitope peptide as taught by the references.

With regard to the limitation "wherein the CpG molecule comprises at least one sulfur atom" recited in base claim 1, the phosphorothiate backbone of the CpG molecule is a sulfur containing portion of the CpG molecule.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 6, 8, 16, 20 and 24 stand provisionally rejected on the ground of nonstatutory double patenting over claims 1-4, 7, 9-11, 13-16, 18-21, 24-26 and 30-33 of copending Application No. 11/513,628 in view of Schirmbeck *et al* (J. Immunol. 2003, 171: 5198-5207, IDS reference) and Vives *et al* (J. Biol. Chem. 1997, 272(25): 1610-1617, IDS reference).

This is a provisional obviousness-type double patenting rejection.

The claims of copending Application No. 11/513,628 are drawn to a composition comprising a polypeptide and a CpG molecule, wherein said polypeptide is a fragment of a full-length polypeptide, and wherein said fragment comprises a CTL-activating amino acid sequence and a CpG-interacting amino acid sequence, wherein said CpG-interacting amino acid sequence comprises at least one cysteine residue, and including the limitations recited in the dependent claims.

Claims of copending Application No. 11/513,628 differ from the instant claims in that the polypeptide of the instant claims is not a fragment of a full-length polypeptide (*i.e.,* comprised of homologous elements), but is rather comprised of heterologous elements, *i.e.,* a CTL-activating sequence and a CpG-interacting sequence.

Schirmbeck *et al* teach administering a composition comprising a polypeptide comprising a CTL activating amino acid sequence that is a class I MHC-restricted peptide epitope covalently linked to a heterologous cationic amino acid sequence that binds to CpG, and further comprising CpG. Schirmbeck *et al* teach that other antigenic peptides, including the tumor antigen peptide SV40 T, also functioned in CTL priming when linked covalently to a CpG-binding sequence and administered with CpG. Schirmbeck *et al* teach that the sequence of the T4 peptide is VVYDFLKCMVYNI and that it is fused to the heterologous peptide cationic HIV Tat peptide PKKRRQRRR. Schirmbeck *et al* teach that fusing this epitope or others, including CTL antigenic epitopes such as SIINFEKL or VWLSVIWM, to cationic peptides bound to immune-stimulating ISS+ ODN (*i.e.,* with CpG-containing sequences, with or without a phosphorothiate backbone, *i.e.,* has a sulfur atom instead of one of the non-bridging oxygen atoms) generated immunogens that efficiently primed long-lasting, specific CD8+ T cell immunity of high magnitude. Schirmbeck *et al* teach that ODNs bind cationic peptides with positively charged side groups, *i.e.,* R or K, for example. Schirmbeck *et al* teach that cationic R-rich peptides interact with their guanidine head groups through H bonds with the negatively charged phosphate backbone of RNA or DNA molecules. Schirmbeck *et al* teach that these cationic peptides are described as protein translocation domains or cell-penetrating peptides, and the process of uptake of ODN by cells is sequence independent and involves receptor-mediated endocytosis (see entire reference).

Vives *et al* teach that the Tat 48-60 peptide (CGRKKRRQRRRPPQC) with both a N- and a –C-terminal cysteine and with or without the three carboxy-terminal amino acid residues (CGRKKRRQRRRC) induced good intracellular translocation of the peptide. Vives *et al* further teach that the cysteines allow coupling to fluorochromes or to peptides, proteins, oligonucleotides or peptide- nucleic acids to improve the cellular uptake and induce a biological activity (see entire reference, especially abstract, materials and methods, and discussion section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a composition such as recited in the claims of copending Application No. 11/513,628 except using heterologous elements for the CTL-activating amino acid sequence and the CpG-interacting sequence and additionally, to have substituted any cationic translocating peptide such as the Tat peptide taught by Vives *et al* having two cysteine residues for the Tat peptide taught by Schirmbeck *et al* in the fusion construct taught by Schirmbeck *et al* or to have made a conjugate comprising an antigenic CTL epitope such as taught by Schirmbeck *et al* and further comprising the Tat peptide taught by Vives *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to use CTL activating amino acid sequences that don't naturally comprise contiguous sequence that is CpG-interacting, and in addition, with regard to Tat peptide taught by Vives *et al,* for convenience sake in order to couple the peptide to a fluorochrome, a peptide, a protein, an oligonucleotide or a peptide- nucleic acid complex as taught by Vives *et al.*

8. Claims 1-3, 6, 8, 16, 20 and 24 are directed to an invention not patentably distinct from claims 1-4, 7, 9-11, 13-16, 18-21, 24-26 and 30-33 of commonly assigned 11/513,628 as enunciated supra.

9. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/513,628, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the Examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

10. Dependent claim 13 is free of the art of record.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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